ERCC2/XPD Polymorphisms and Lung Cancer Risk

To the Editor:

I read with interest, the recently published meta-analysis by Zhan et al.,[1] involving 22 case-control studies of the excision repair cross-complimenting rodent repair deficiency, complementation group 2 (*ERCC2/XPD*) polymorphisms and lung cancer risk. Nevertheless, there is one error in the article that diminishes the findings and conclusions considerably.

The authors cite in Table 1 that our study, the largest among the 22 analyzed, comprised Asian (Chinese) ethnicity.[2] Nevertheless, although the first author of this article from my research group is a Chinese national, the population was 100% white from the New England region of the United States. Hence, the results presented in Figures 1 and 2 are incorrect and should be recalculated. Moreover, the interpretation of results and conclusions should be also revised accordingly.

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Disclosure: The author declares no conflicts of interest.
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In Response:

Because of our carelessness, we made a mistake about the ethnicity (country of origin) of the study by Zhou et al.[1] The population in the study by Zhou et al.[1] was Caucasian from the United states; however, in our study,[2] it was stated as Asian (Chinese). Hence, we had to recalculate the meta-analysis results according to the ethnicity subgroup analysis.

For the Xeroderma Pigmentosum group D (XPD) *Lys751Gln* genotype, when stratified by ethnicity, significantly increased risks were found among Caucasians for both the homozygote CC versus AA (odds ratio [OR] = 1.30, 95% confidence interval [CI] = 1.15–1.48; p = 0.923 for heterogeneity) and the C allele carriers versus AA (OR = 1.21, 95% CI = 1.16–1.58; p = 0.358 for heterogeneity). Among Asians, no significant association was found in homozygote CC versus AA (OR = 1.07; 95% CI = 0.67–1.72; p = 0.194 for heterogeneity) or for the C allele carriers versus AA (OR = 1.14; 95% CI = 0.73–1.62; p = 0.278 for heterogeneity) (Figure 1).

For the XPD *Asp*312*Asn* genotype, when stratified by ethnicity, significantly increased risks were found among Caucasians for both the homozygote AA versus GG (OR = 1.20, 95% CI = 1.05–1.38; p = 0.460 for heterogeneity) and the A allele carriers versus GG (OR = 1.34, 95% CI = 1.11–1.74; p = 0.374 for heterogeneity). Among Asians, significantly increased risks was also found with homozygote AA versus GG (OR = 5.07; 95% CI = 2.09–12.34; p = 0.049 for heterogeneity) or the A allele carriers versus GG (OR = 4.54; 95% CI = 1.83–8.52; p = 0.374 for heterogeneity) (Figure 2).

When stratified according to ethnicity, different results were found between Asians and Caucasians for the XPD *Lys*751*Gln* genotype but not *Asp*312*Asn* genotype. For the XPD *Lys*751*Gln* genotype, significantly increased risks were identified among Caucasians for both the homozygote CC versus AA and the C allele carriers versus AA. Among Asians, however, no significant association was found in homozygote CC versus AA or the C allele carriers versus AA, which was consistent with our previous study.[2] For the *Asp*312*Asn* genotype, the increased risks were apparent with not only Caucasians but Asians for both the homozygote CC versus AA and the C allele carriers versus AA, which was consistent with the results of the meta-analysis study by Zhang et al.[3] These findings indicated that polymorphisms of XPD may be important in regard to specific ethnicity of patients with lung cancer and that XPD *Lys*751*Gln* may differentially affect individuals of different ethnic genetic backgrounds for risk of lung cancer. Population stratification is an area of concern in any complex disease association study as it can confound the linkage results between a molecular marker and phenotype.[4] The observed ethnic differences may also be a result of chance because studies with small sample size are likely to be insufficiently powered to detect a slight effect. In addition, the heterogeneity test among Asians studies for XPD *Asp*312*Asn* genotype was significant. Considering the limited studies and population numbers of Asians studies in this meta-analysis, our results among Asians should be interpreted with caution. Hence, large case-control studies on the association between the XPD gene polymorphism and lung cancer risk among Asians should be conducted in the future.

In summary, this meta-analysis suggested that the XPD *Lys*751*Gln* and *Asp*312*Asn* gene polymorphisms were associated with lung cancer risk; the C allele of XPD *Lys*751*Gln* genotype was an increased risk factor for developing lung cancer among Caucasians, and the A allele of the XPD 312 genotype was also an increased risk factor for developing lung cancer among Asians and Caucasians.

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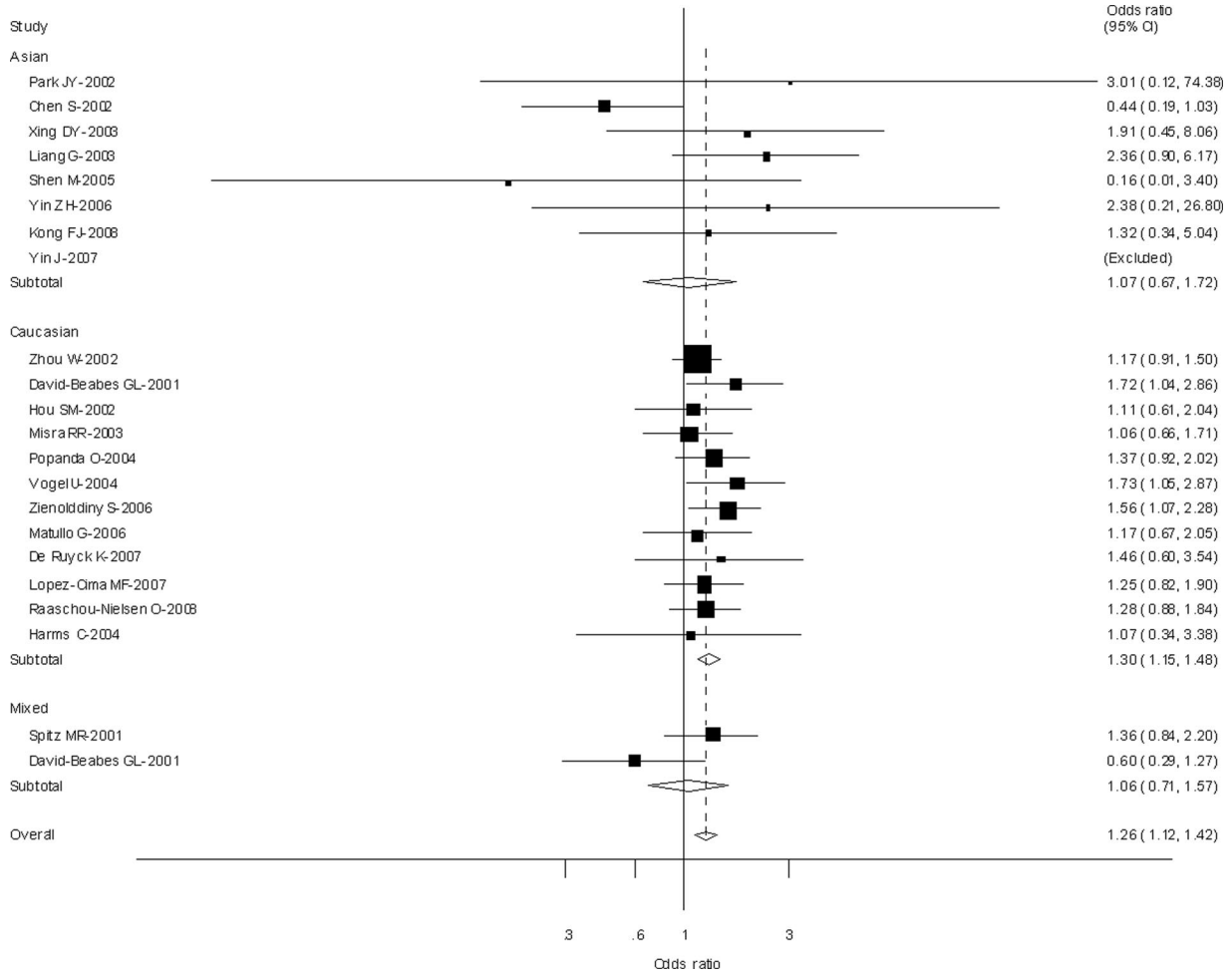

FIGURE 1. Forest plot (random-effects model) of lung cancer risk associated with XPD *Lys751Gln* genotype for CC versus AA. Each box represents the OR point estimate, and its area is proportional to the weight of the study. The diamond (and broken line) represents the overall summary estimate, with CI represented by its width. The unbroken vertical line is set at the null value (OR = 1.0). OR, odds ratio.

velopment Foundation (Molecular Predictor of Personalized Therapy for Chinese Patients with Non-small Cell Lung Cancer) (Lk-Yu).

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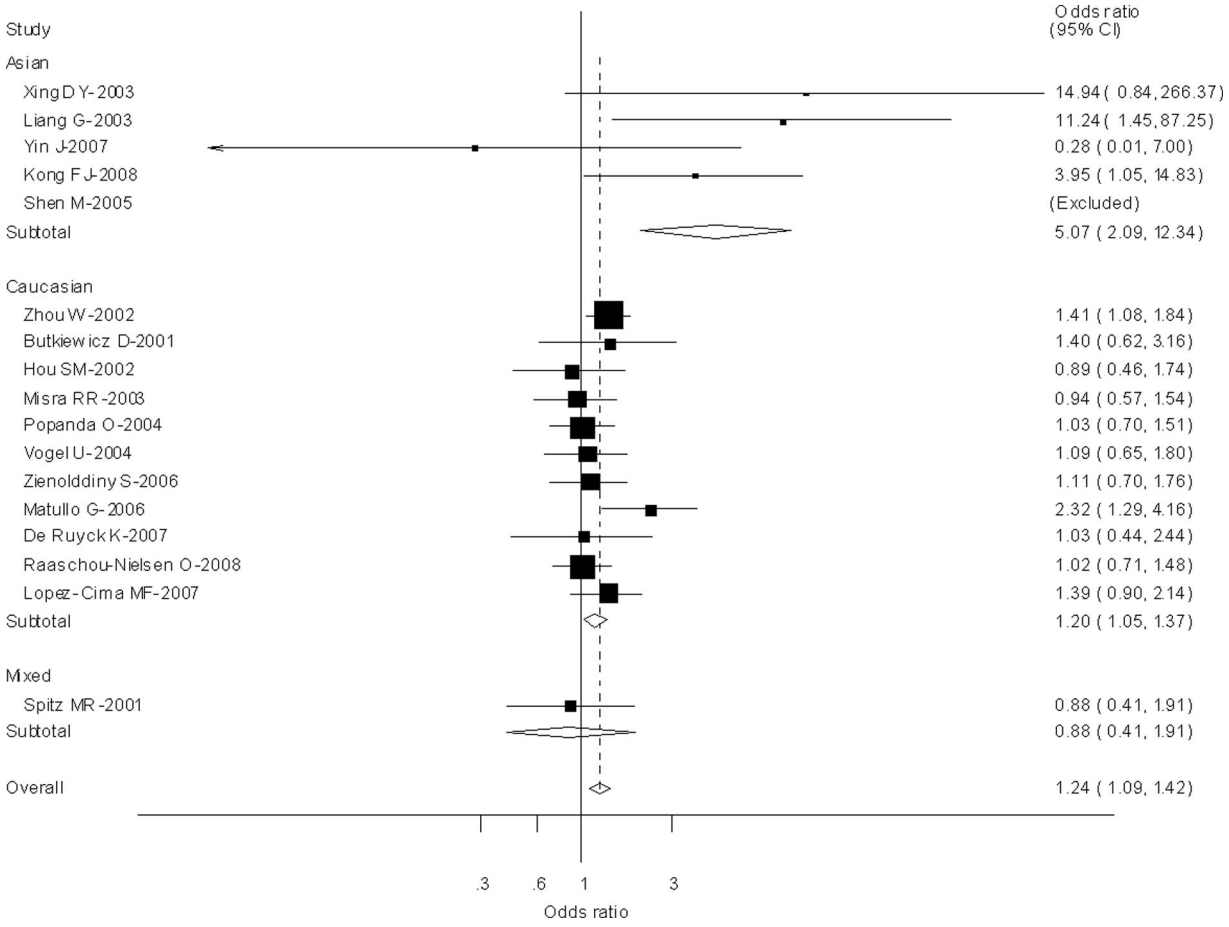

FIGURE 2. Forest plot (random-effects model) of lung cancer risk associated with XPD *Asp*312*Asn* genotype for AA versus GG.